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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BOESEN, AGNIESZKA	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/807,506	SMIT ET AL.	
	Examiner	Art Unit	
	Agnieszka Boesen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-142* is/are pending in the application.

4a) Of the above claim(s) *112-132,134,135 and 142* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94-111, 133, 136-141* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is responsive to the communication received February 23, 2007. The Final Rejection of April 19, 2004 is vacated. Applicant's election in response to restriction requirement of May 24, 2006 is acknowledged. The prosecution is hereby reopened.

Election/Restrictions

Applicant's election with traverse of group I, claims 94-111, 133, and 136, the species of electrospray mass spectroscopy, signal peptides and signal proteins, and zinc binding signal peptides is acknowledged.

Applicants argue that the Katre et al. (WO 88/01511) document cited in the restriction requirement of May 24, 2006, does not furnish substantial evidence to support the restriction requirement. Applicants argue that Katre does not teach the specific limitations of the current claims. It is noted that the present claims were deemed to lack unity of invention because Applicant's invention does not contribute a special technical feature when viewed over the prior art. Thus, because Katre teaches the special technical feature of the present invention, as discussed in the restriction requirement of May 24, 2006, the restriction is deemed proper and is made FINAL.

Claims 137-142 have been added. Claims 112-132, 134, 135, and 142 are withdrawn because the claims are drawn to the non-elected invention. Claims 94-111, 133, 136-141 are under examination in the present Office action.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 110 recites the limitation "the substrate". There is insufficient antecedent basis for this limitation in the claim.

Claims 94-111, 133, 136-141 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 94 recites "monitoring the modification reaction with a mild and sensitive method such as non denaturing electrophoresis". The specification does not provide a definition for the claimed mild and sensitive method. It is known in the art that the ingredients and method steps for the general electrophoresis method may vary depending on various factors such as for example the type of protein being studied. The recitation of a mild and sensitive method without the definition of the phrases "mild" and "sensitive" in the specification renders the claims vague and indefinite. The claim recites that the mild and sensitive method is a non-denaturing electrophoresis. However it is not clear what exact conditions/ ingredients should be necessarily used in order for the method to be mild and sensitive. Thus because the metes and bounds of the terms "mild" and "sensitive" cannot be determined and the definition for those terms cannot be

found in the present specification, the claims are therefore indefinite. Clarification and correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 94-100, 104-106, 109, 133, 136, 137, and 140 are rejected under 35 U.S.C. 102(b) as being anticipated by Witkowska et al. (Hemoglobin, 1993, Vol. 17, p. 227-242).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, mass spectrometry and/or assaying biological activity of the modified product. The proteins or peptides are zinc binding signal peptides and signal proteins. The chemical modification comprises alkylation using iodo acetate and it is conducted under conditions comprising pH range between pH of 5.0 and 7.0. The modification comprises adding chelating agent such as urea.

Witkowska et al. disclose a method of quantitative structure function analysis of a chemically modified proteins such as zinc binding protein hemoglobin comprising monitoring the modification reaction using a method of electrospray mass spectrometry (see the entire document, particularly Materials and Methods, page 231, and Figure 1). Witkowska et al. disclose using mass spectrometry to analyze the protease treated (trypsin treated) hemoglobin peptide chains (see Materials and Methods, page 229). Witkowska et al. disclose chemical modification of hemoglobin comprising alkyltion with iodo acetate and addition of urea as chelating agent. The chemical modification of hemoglobin is conducted under conditions comprising pH range between pH of 3.0 to 7.5, which encompasses the currently claimed pH range between 5.0 and 7.0 (see Materials and Methods, page 229-230). Thus by this disclosure Witkowska et al. anticipate the current claims.

Claims 94-100, 106, 109, and 138 are rejected under 35 U.S.C. 102(b) as being anticipated by Knepper et al. (Biochemistry, 1992,Vol. 31, p. 11651-11659).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, mass spectrometry and/or assaying biological activity of the modified product. The proteins or peptides are zinc binding signal peptides and signal proteins such as interleukins, particularly IL-3.

Knepper et al. disclose a method of quantitative structure function analysis of a chemically modified IL-3, comprising monitoring the modification reaction using a method of

electrospray mass spectrometry (see the entire document, particularly Experimental procedures on page 11652, and Figure 8). Knepper et al. disclose using mass spectrometry to analyze the protease treated (tryptic digest) deglycosylated IL-3a (see page 11653, second column, page 11656 – 11657, Table 1, and Figures 3-7). Thus by this disclosure Knepper et al. anticipate the current claims.

Claims 94-100, 106, and 109 are rejected under 35 U.S.C. 102(b) as being anticipated by Arcone et al. (European Journal of Biochemistry, 1991, Vol. 198, p. 541-547).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, mass spectrometry and/or assaying biological activity of the modified product. The proteins or peptides are zinc binding signal peptides and signal proteins such as interleukins.

Arcone et al. disclose a method of quantitative structure function analysis of a chemically modified IL-6, comprising monitoring the modification reaction using a method of electrospray mass spectrometry (see the entire document, particularly Materials and Methods). Arcone et al. disclose using mass spectrometry to analyze the protease treated (trypsin digested) IL-6 (see page 543, Peptide mapping). Thus by this disclosure Arcone et al. anticipate the current claims.

Claims 94-100, 106, and 109 are rejected under 35 U.S.C. 102(e) as being anticipated by Woods (US Patent 5,658,739).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, mass spectrometry and/or assaying biological activity of the modified product. The proteins or peptides are zinc binding signal peptides and signal proteins.

Woods discloses a method of quantitative structure function analysis of a chemically modified proteins such as zinc binding protein hemoglobin comprising monitoring the modification reaction using a method of electrospray mass spectrometry (see column 7, lines 26-61, column 9, lines 34-56, column 12, lines 18-25, column 22, lines 40-56, and Examples columns 24-25). Woods disclose using mass spectrometry to analyze the protease treated (proteolytically digested) proteins (see column 22, lines 40-56). Thus by this disclosure Woods anticipates the current claims.

Claims 94-100, 106, 109, and 138 are rejected under 35 U.S.C. 102(e) as being anticipated by Braford-Goldberg et al. (US Patent 5,501,962).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, mass spectrometry and/or assaying biological activity of the modified

product. The proteins or peptides are zinc binding signal peptides and signal proteins such as interleukins, particularly IL-3.

Braford-Goldberg et al. disclose a method of quantitative structure function analysis of a chemically modified IL-3 comprising monitoring the modification reaction using a method of electrospray mass spectrometry (see the entire document, particularly column 16, lines 42-65). Braford-Goldberg et al. disclose assaying biological activity of the modified product using mass spectrometry (see column 18, lines 30-67, and Table 1 in column 19). Thus by this disclosure Braford-Goldberg et al. anticipate the current claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 101-103 are rejected under 35 U.S.C. 103(a) 138 as being unpatentable over Knepper et al. (Biochemistry, 1992,Vol. 31, p. 11651-11659); Arcone et al. (European Journal of Biochemistry, 1991, Vol. 198, p. 541-547); Woods (US Patent 5,658,739); and Braford-Goldberg et al. (US Patent 5,501,962) as applied to claims 94-100, 106, 109, and 138 and further in view of Weber et al. (US Patent 5,710,252) and Rosnack et al. (Rapid Communication in Mass Spectrometry, 1992, Vol. 6, p. 637-640).

Claims are drawn to a method for quantitative structure function analysis research on biologically active proteins or peptides comprising gradual chemical modification of a protein or peptide, monitoring the modification reaction using a method of electrospray mass spectrometry, protease treatment, wherein the protease is endoprotease Endo Glu C, Endo Lys C, and exoprotease such as carboxypeptidase Y.

Knepper et al., Arcone et al., Woods and Braford-Goldberg et al. teach the electrospray mass spectrometric analysis of proteolitically digested proteins as discussed above. The references do not expressly teach particular proteases such as endoprotease Endo Glu C, Endo Lys C, and exoprotease such as carboxypeptidase Y.

Weber et al. teach using endoproteases such as trypsin, pepsin, Endo Glu C, and Endo Lys C for protein and polypeptide digestion (see column 8, lines 63-67, and column 9, lines 1-6). Rosnack et al. teach sequencing of peptides digested with carboxypeptidase Y using electrospray mass spectrometry (see the entire document).

It would have been obvious to the person of ordinary skill in the art to use endoprotease Endo Glu C, Endo Lys C, and exoprotease such as carboxypeptidase Y to digest peptides and proteins for subsequent spectrometric analysis.

The skilled artisan would have been motivated to use Weber's and Rosnack proteases in the methods of Knepper et al., Arcone et al., Woods and Braford-Goldberg et al., because Rosnack teaches that using carboxypeptidase Y allows to monitor the course of peptide digestion while using electrospray and other mass spectral techniques (see page 637 left column).

One would have had a reasonable expectation of success to use Weber's and Rosnack's proteases in the methods of Knepper et al., Arcone et al., Woods and Braford-Goldberg et al.,

because those proteases have been successfully used for digestion of peptides and proteins as evidenced by Weber and Rosnack.

Therefore, the invention as a whole would have obvious to one of ordinary skill in the art at the time the invention was made.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Bauer et al. (US Patent 5,677,149 and US Patent 5,817,486) disclose mass spectrometric analysis of the chemical modifications of IL-3.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnieszka Boesen whose telephone number is 571-272-8035. The examiner can normally be reached on 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AB

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